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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/945,144	01/20/1998	MICHEL LEBRUN	RP/PCT	2339

7590

08/28/2002

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EXAMINER

KRUSE, DAVID H

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 08/28/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/945,144

Applicant(s)

LEBRUN ET AL.

Examiner

David H Kruse

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2002 and 20 May 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 44 is/are allowed.
- 6) ☒ Claim(s) 42,45,46 and 50-54 is/are rejected.
- 7) ☒ Claim(s) 43 and 47-49 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. The Amendments filed 10 May 2002 as Paper No. 28 and the Supplemental Amendment filed 20 May 2002 as Paper No. 29 have been entered into the application.
2. Claims 42-54 are pending.
3. The rejection of claim 44 under 35 U.S.C. § 101 is withdrawn in view of Applicant's amendment to said claim.
4. The pending objections to claims 43, 46, 48, 51 and 52 are withdrawn in view of Applicant's amendments to said claims.
5. The rejection of claims 48, 49, 51 and 52 under 35 U.S.C. § 112, second paragraph, as indefinite is withdrawn in view of Applicant's amendments to said claims.
6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

7. Claims 42, 46, 47, 50, 53 and 54 are objected to because of the following informalities:

At claim 46, line 1, the phrase "comprising nucleic acid" lacks an article of language and should read -- comprising a nucleic acid --.

At claim 52, line 4, the phrase "crop seed or plant" should read -- crop seeds or plants -- in order to be in number agreement with the same phrase at line 3.

At claims 42, 47, 50, 53 and 54, the phrase "of mature EPSPS sequence" is objected to because it lack a definite article of language and should read -- of the mature EPSPS sequence --.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

8. Claim 54 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Specifically a plant comprising a mature EPSPS protein of plant origin having the claimed substitutions reads on a naturally occurring mutant plant, which is product of nature. Amending the claim to read -- A plant transformed with a nucleic acid encoding a mature EPSPS protein -- would obviate this rejection.

Claim Rejections - 35 USC § 112

9. Claim 42 remains rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, Applicant has only described a modified maize EPSPS encoding polynucleotide having the claimed modifications. This rejection is repeated for the reason of record as set forth in the last Office action mailed 20 November 2001. Applicant's arguments filed 10 May 2002 have been fully considered but they are not persuasive.

Applicant argues that because the specification describes two specific mutations in the maize EPSPS enzyme, that all other plant EPSPS enzymes having the claimed mutations have been adequately described, thus having the implied tolerance to glyphosate (see page 8 of the Remarks). This argument is not found to be fully persuasive because Applicant does not adequately describe the claimed invention such

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that one of skill in the art would have recognized that Applicant was in possession of the invention as broadly claimed. Applicant describes that the claimed substitutions can be introduced or be present in an EPSPS sequence of any origin, in particular of plant, bacterial, algal or fungal origin (see paragraph spanning pages 3-4). Yet, Applicant does not provide any description of common features of this diverse genus of EPSPS enzymes, or nucleic acids encoding them, that would lead one of skill in the art to recognize the claimed invention. In particular, Applicant does not describe and align other plant nucleic acids encoding EPSPS known at the time of filing, and describe a consensus sequence, or location of respective codons that could be mutated in other plant EPSPS nucleic acids. Also, it does not appear that Applicant contemplated the claimed invention as limited to plant EPSPS enzyme encoding nucleic acids, and excluding other EPSPS nucleic acids, hence there is no evidence that Applicant was in possession of the invention as broadly claimed.

The DeRose Declaration, presumed to have been submitted under 37 CFR § 1.132 and filed 10 May 2002, is insufficient to overcome the rejection of claim 42 based upon 35 U.S.C. § 112, first paragraph, for written description as set forth in the last Office action because: The DeRose Declaration does not overcome the deficiency of written description in the instant Application. The DeRose Declaration states on page 6, paragraph 15, that "all known plant EPSPS enzymes were known to have the identical conserved region and that it was apparent that any plant EPSPS enzyme was essentially interchangeable with any other EPSP enzyme, the only possible conclusion that any person of ordinary skill in the art could reach is that the disclosed EPSPS

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mutations would be applicable to every plant EPSPS enzyme". Applicant's evidence of similarities between the disclosed maize EPSPS enzyme amino acid sequence and that of other plant EPSPS enzymes appears to have been subsequent to Applicant's invention, hence does not describe the general knowledge of one of skill in the art at the time of Applicant's invention (see page 3, paragraph 7 of the DeRose Declaration). The DeRose Declaration's reference to the '908 patent of Kishore *et al* on page 3, paragraph 7, does not remedy the issue because Kishore, in Figure 2, does not disclose the Pro₁₀₆ of the maize EPSPS enzyme as conserved among all known EPSPS enzymes, and Kishore is directed to mutating the second Glycine in the sequence -L-G-N-A-G-T-A- to an Alanine to produce glyphosate resistance.

10. Claims 42, 45, 46 and 50-53 remain rejected and claim 54 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide of maize origin encoding a modified 5-enolpyruvylshikimate-3-phosphate synthase having the claimed modifications, vectors, transgenic plants and plant cells comprising said DNA sequence, and a method of protecting plants comprising said transgenic plants, does not reasonably provide enablement for all isolated polynucleotides of plant origin encoding a modified 5-enolpyruvylshikimate-3-phosphate synthase having the claimed modifications, vectors, transgenic plants and plant cells comprising said DNA sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is repeated for the reason of record as set forth in the last Office action mailed 20

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November 2001. Applicant's arguments filed 10 May 2002 have been fully considered but they are not persuasive.

Applicant argues that the general nature of the invention is the obtaining of glyphosate tolerant EPSPS enzymes, and that the claims here are relatively narrowly directed to a plant EPSPS enzyme (page 11, 1st paragraph of the Remarks). Applicant argues that as evidenced by the cited prior art and as set forth in the DeRose Declaration, the state of the prior art with respect to EPSPS structure, its function in plants, decoding of the specific sequences, methods of mutating EPSPS, transformation of plants with EPSPS constructs to obtain glyphosate tolerance, and the like was fairly well-developed at the time the subject invention was made (see page 11, 2nd paragraph of the Remarks). Applicant argues that the level of skill in the art is evident by the many issued patents and applications in this art that, by 1995, the design of vectors for introducing glyphosate tolerance into plants, and plant transformation with such vectors, was essentially routine (see page 11, 3rd paragraph of the Remarks). Applicant states that prior to the subject invention, whether a given mutation or combination of mutations in an EPSPS sequence will provide glyphosate tolerance was arguably unpredictable, however, once certain mutations in a plant EPSPS were established to provide glyphosate tolerance it was relatively predictable that the same mutations in other plant EPSPS sequences would also work (see page 11, 4th paragraph of the Remarks). Applicant argues that given the straightforward nature of the invention in a well-developed art that the working example provides sufficient guidance to make the claimed mutations in any plant EPSPS sequence (see page 12, 3rd paragraph of the

Remarks), and that no undue experimentation would be required to practice the invention within the breadth of the claims (see page 12, 4th paragraph of the Remarks).

The Examiner responds, the DeRose Declaration reiterates the general knowledge of the art at the time of Applicant's invention and subsequent to Applicant's invention (pages 7-11 of the DeRose Declaration). The DeRose Declaration only demonstrates that one other EPSPS enzyme-encoding gene has subsequently been mutated to produce the claimed invention, citing WO 00/66746 published 9 November 2000 (see pages 9-10 of the DeRose Declaration). The demonstrations that a single, subsequent instance of success in producing the claimed invention does not enable the invention within the full scope of the claims. The issue of the skill of the art at the time of Applicant's invention in producing plant transformation vectors and transforming plants therewith is not relevant. It is the issue of producing a glyphosate resistant plant EPSPS encoding gene. The predictability demonstrated by the art at the time of Applicant's invention was directed to mutating any EPSPS encoding gene, not just plant genes, to produce glyphosate resistant EPSPS enzymes. It is clear from the prior art that not all EPSPS enzymes comprise a Pro₁₀₆, especially fungal enzymes, hence the claimed invention was not enabled for all EPSPS encoding genes at the time of Applicant's invention. Even considering the '908 patent of Kishore *et al* as discussed *supra*, Kishore demonstrated functional mutation of multiple plant EPSPS enzymes. The nature of the claimed invention is such that extensive guidance would have been required, or a demonstration of diligence on the part of Applicant to demonstrate that a gene encoding any mutated plant EPSPS enzyme as claimed would in fact produce a

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glyphosate EPSPS enzyme. It was well known in the art at the time of Applicant's invention that substituting amino acids in the amino acid sequence of an enzyme has an influence on the secondary and tertiary structure of said enzyme and thus on the function of said enzyme. Hence, it is unclear that Applicant has enabled the invention as broadly claimed.

Concerning new claim 54, said claim appears to encompass a plant produced by a method of *in situ* mutagenesis or other technology, either not known or contemplated at the time of Applicant's invention, or not perfected in plants at the time of Applicant's invention (see for example Hohn and Puchta 1999, Proceedings of the National Academy of Science 96:8321-8323). In addition, Hohn and Puchta teach that it requires extensive guidance to use *in situ* modification of genes in plants (see page 8322, paragraph spanning columns). Hence, claim 54 is not enabled for a plant comprising a mature EPSPS protein of plant origin having the claimed amino acid substitutions except for such a plant produced by a plant transformation method.

Allowable Subject Matter

11. Claims 47-49 are allowable upon correction of the claim objection of claim 47 as discussed supra.

12. Claim 43 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. Claim 44 is allowed.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Kim Davis whose telephone number is (703) 305-3015.

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized, flowing script.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

David H. Kruse, Ph.D.
19 August 2002